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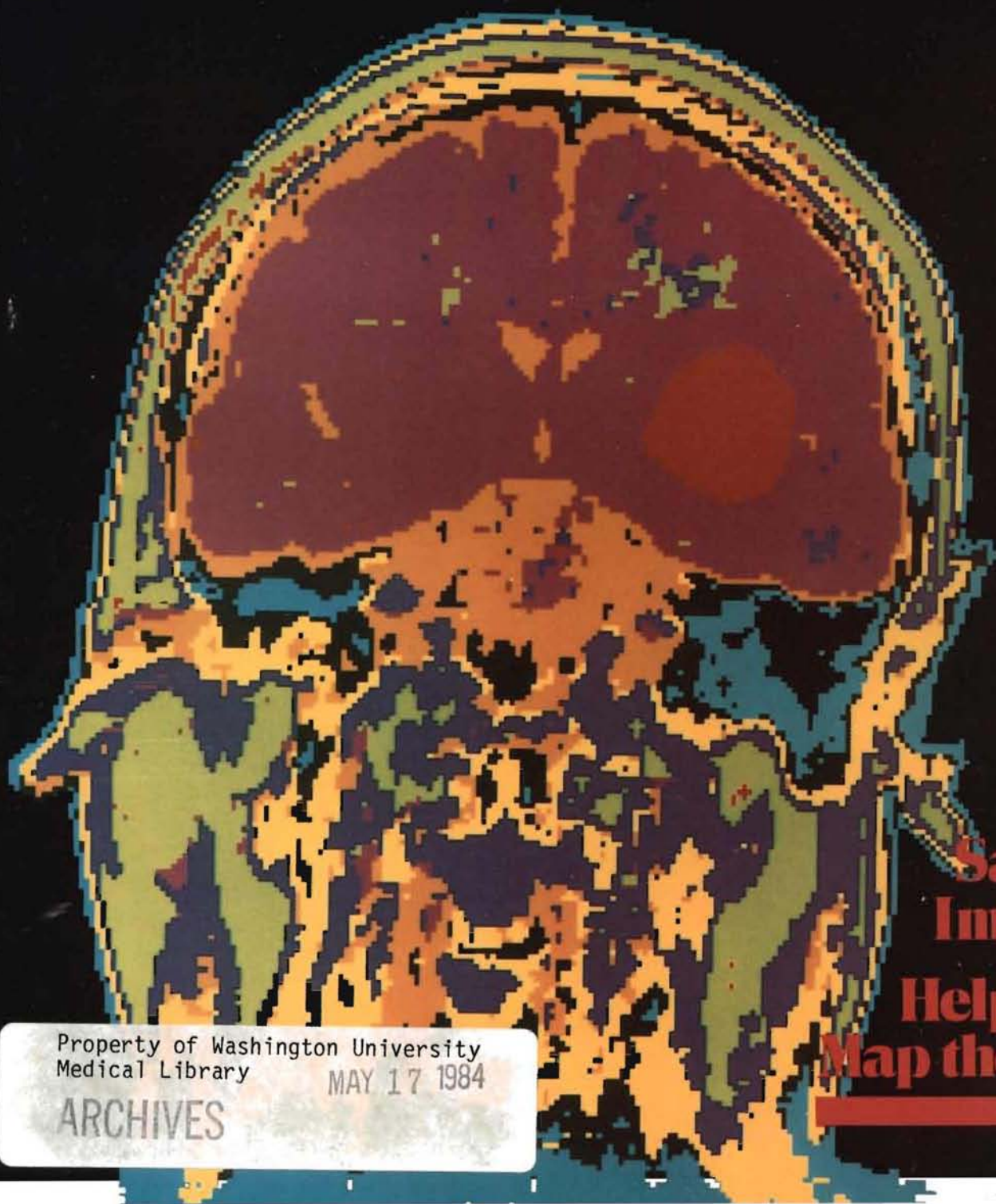
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Washington University School of Medicine

Winter 1984

OUTLOOK

M A G A Z I N E



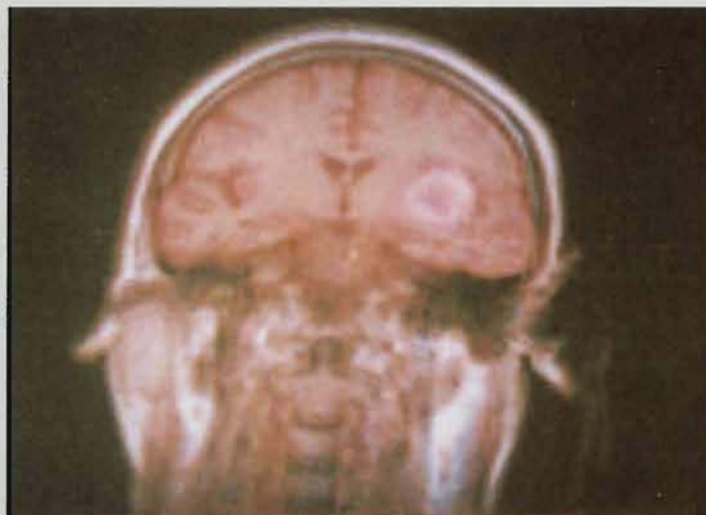
**Satellite
Imaging:
Helping to
Map the Body**

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NASA Imaging Applied to NMR Scanning



In the Satellite Imaging story beginning on page seven, researchers tell how NASA imaging technology is being applied to NMR scanning. Above, two satellite images of Lake Okeechobee (right) are placed beside two NMR scans (left) for comparison. The top images are color composites, which are judicious combinations of several images created

under different conditions. The bottom images are "theme maps," in which various components are color-keyed. Water, marsh and land are identifiable in the Lake Okeechobee map. In the theme map of the head, grey and white matter of the brain are colored green and blue, respectively.

OUTLOOK

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On The Cover:

This color-keyed map was created when LANDSAT satellite imaging technology was used to analyze several nuclear magnetic resonance (NMR) scans of a patient's head. The red circle indicates the location of a blood clot which has formed in one of the cerebral hemispheres. Each color indicates a particular type of tissue. Orange, for example, is cerebrospinal fluid.

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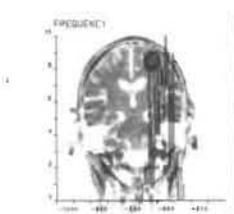
Elisa

2



Help for the Heart

4



Satellite Imaging

7



Evarts A. Graham Symposium

10



Samuel Becker Grant, M.D.

12



Newsbriefs

16

The Alumni Report

21

elisa

B Y K A T H Y L I S Z E W S K I

Numerous laboratories throughout the country, including several at Washington University School of Medicine, have begun employing a new research and clinical assay system which harnesses enzymes as biological signalers. The rapidly emerging technology is called ELISA, pronounced "ee-LIE-zah," and stands for Enzyme Linked Immunosorbent Assay.

Similar to traditional tests which employ antibodies and their corresponding antigens, the use of enzymes and their partner substrates as "tags" represents a major advance in diagnostic and research testing.

Although many traditional clinical tests utilize other types of tags, several problems exist with these assays. Some of the best established methods involve fluorescent tags which "glow" when illuminated under a microscope. However, these tests are time consuming, not easily automated, subject to operator interpretation, and not readily quantifiable.

Another classical test, radioimmunoassay, employs radioactive isotopes as tags. While highly sensitive and automatable, this assay has problems such as the hazards of handling and disposing of radioactive substances, short shelf life of the costly reagents, and expensive, complex equipment required for analysis.

Now enter the ELISA. This method overcomes many of the disadvantages of immunofluorescence and radioimmunoassay, yet combines the advantages. Enzyme-labeled reagents are safe, cheap to prepare, stable for long periods, yet are as sensitive as radioimmunoassay. Additionally, they yield objective results detectable visually and quantifiable with relatively simple equipment.

Numerous variations of the ELISA exist both in protocol and in enzyme-substrate system employed. (See "Enzyme Immunoassay ELISA and EMIT" by Eva Engvall in *Methods in Enzymology* Vol. 70, Part A, p. 419, Academic Press, 1980.)

As illustrated in the diagram, a common method called the "Double Antibody Stacking ELISA" detects the presence of specific types of antibodies.

Antigens, to which the corresponding antibody will bind, are placed in plastic 96-well microtiter plates. The antigen becomes tightly attached to the surface of the wells. When test samples thought to contain the specific antibody are incubated within the wells, any antibody present binds the antigen. After washing steps to free nonbound material, an added enzyme-tagged "second" antibody will



Gregory Storch, M.D., checks specimens for the presence of rotavirus by using his laboratory's ELISA reader.

bind to any first antibody present. Finally, adding the enzyme's substrate will cause a color to develop in direct proportion to the amount of antibody present.

This particular application of ELISA technology allows detection of autoimmune antibodies. Patients who suffer from diseases such as rheumatoid arthritis and lupus erythematosus possess antibodies against components of their own bodies. Theodore Munns, Ph.D., research assistant professor of medicine, rheumatology division, has developed an ELISA method which can pinpoint autoimmune antibodies which react to the individual constituents of DNA (i.e., nucleotides).

In his version of the ELISA, Munns and associates apply the basic components of DNA to the test well. Incubating a patient's serum within the coated well allows any antibodies present in the serum to bind the compound adhering to the solid plastic walls. After rinsing the well, all other components are washed free, leaving only the antibody/antigen complexes. These are pinpointed by adding an enzyme-tagged anti-human antibody to the test well. This second antibody will bind to any human antibody that is present. After addition of the substrate, a color will emerge if a reaction has occurred. This, then, provides a test for detecting specific types of autoimmune antibodies.

"By looking at which components of genetic material a patient's serum attacks, we would like to find certain patterns related to particular diseases," Munns said. "For example, early data with ELISA suggest that patients with scleroderma possess higher amounts of antibodies to uridine, one of the five components of nucleic acids. Whether this will hold true for a large sampling of such patients remains to be seen. Pinpointing what autoimmune antibodies are binding could provide answers to the etiology of the disease, and may also suggest new therapies."

Similar use of the ELISA to detect antibodies has been applied by Associate Professor Julian Fleishman, Ph.D., and Ms. Donna Thurmond in the Department of Immunology and Microbiology. Their laboratory provides expertise in establishing a suitable ELISA for use by any investigator who is developing monoclonal antibodies at the Hybridoma Center. Additionally, they assist researchers by determining which particular variety, i.e., isotype, of monoclonal antibody has been selected.

According to Fleishman, "We find that ELISAs are much more convenient, less expensive, and adaptable to a variety of tests. They are particularly useful when processing large numbers of samples."

In another application of this technology, Howard Welgus, M.D., assistant professor of medicine, dermatology division, has recently developed an ELISA to examine a protein called human skin collagenase inhibitor. Collagen, probably the most widespread and abundant protein in the animal kingdom, is the main protein of skin, tendons and bones. Enzymes which break down collagen are called "collagenases." A substance called "collagenase inhibitor" keeps the activity of collagenase at appropriate levels. So, a delicate system of checks and balances moderates optimum levels of these compounds in a healthy body.

Welgus and associates have developed an ELISA to measure nanogram levels of collagenase inhibitor in human serum, cultured cells and even amniotic fluid. (A nanogram is a billionth of a gram.)

"We are using our ELISA to screen the serum of patients with various systemic diseases, and are looking for a possible link to collagenase inhibitor. For example, the fibrosing diseases, such as idiopathic pulmonary fibrosis, are characterized by excess deposits of collagen and lead to organ dysfunction. Their cause is unknown, but one possibility to investigate is that increased levels of inhibitor could be a contributory factor by allowing more collagen production."

Welgus' group recently discovered that inhibitor levels in the amniotic fluid of

near-term infants are five to six times higher than normal serum concentrations. Welgus speculates that because inhibitor levels rise throughout pregnancy and parallel other tests of lung maturity, quantifying inhibitor levels could provide an ancillary measurement of fetal lung maturity. These tests are critical for estimating the optimum time to perform a needed cesarean delivery.

For the future, Welgus and his associates would like to monitor whether inhibitor and collagenase production are regulated together, and if drugs which affect one will affect the other. They also hope to pinpoint medications which might increase inhibitor levels alone. These could provide new therapies to treat diseases caused or exacerbated by excess collagenase.

Although ELISA methods have become valuable tools for researchers, their greatest utility may be as clinical testing vehicles. Numerous companies are actively pursuing the development and marketing of ELISA kits for the clinical laboratory. Such kits may become the commonplace method of the future because they eliminate the need for radioactivity, possess long shelf lives, and facilitate the economical processing of large numbers of samples.

Already utilizing such tests is Gregory A. Storch, M.D., the director of the microbiology laboratory at Children's

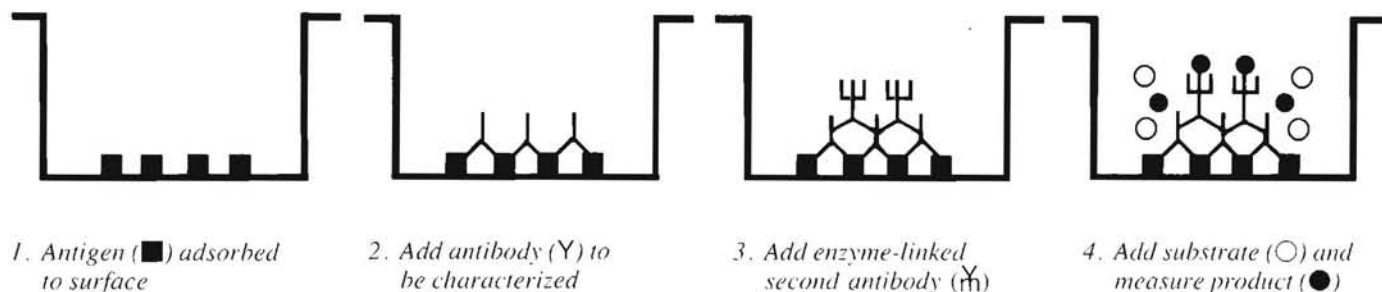
Hospital. An assistant professor of medicine and pediatrics, Storch describes one such ELISA which detects diarrhea-causing rotavirus. This virus was previously detectable in stool specimens only by use of an electron microscope. According to Storch, "The rotavirus ELISA represents a significant advance in the diagnosis of this serious illness. Rotavirus-induced diarrhea is the most common cause of diarrhea which results in hospitalization. And at least 50 percent of all diarrhea-based hospital admissions result from rotavirus alone."

Storch notes that physicians need tests which can rapidly diagnose the presence of viruses and other disease-causing agents. He sees a current fast-paced effort to convert clinical tests into ELISAs, and expects many more to become available soon.

ELISAs are being developed for hormones, drugs, serum components, infectious diseases and a host of other applications.

Worldwide meetings, seminars and workshops have been sponsored by the World Health Organization and international congresses. More are planned in the near future to keep up with the tremendous growth of these methods. Many believe that we have only scratched the surface of ELISA's potential for diagnosing and researching human illness. ■

Double Antibody Stacking Elisa



Schematic representation of ELISA technique utilized for characterizing a wide variety of antibody populations.

HELP

F O R T H E

HEART

B Y D E B B I E F A B I A N

Scientists have discovered that prolonged, intense exercise training can actually strengthen the heart itself in patients with coronary artery disease. In a nation where heart attack is the leading cause of death and disability, those findings perhaps mean more to healthy people, because exercise is more likely to benefit those who haven't yet had damage to the heart.

After evaluating a 12-month program of progressive exercise, researchers at Washington University School of Medicine in St. Louis have concluded that such training can improve heart function in some coronary artery disease patients by increasing blood supply to areas of heart muscle that were not getting enough oxygen. Results were published recently in the journal *Circulation*.

Exercise has already been proven to have peripheral effects, explain Ali A. Ehsani, M.D., and John O. Holloszy, M.D., who headed the study. "It lowers blood pressure and slows heart rate, and generally makes people feel healthier and more capable of physical activity. But until now, there has been no evidence that exercise can help the heart itself in patients with coronary artery disease," Holloszy says. Ehsani is associate professor of medicine and director of the coronary rehabilitation program and Holloszy is professor of medicine and head of applied physiology at Washington University. Both are on staff at Barnes Hospital.

Historically, physicians and cardiologists have prescribed modest exercise programs for victims of heart attack and patients with coronary artery disease, Holloszy says. Patients usually enter a three-month schedule of moderate exercise — 40 minutes of bicycling or walking three times a week — that will condition them to resume their daily normal activities. The Washington University team believed that exercise beyond three months might help the heart even more.

Holloszy, Ehsani, and James Hagberg, Ph.D., an exercise physiologist, decided to test the theory. They enrolled male heart attack victims in year-long exercise

programs that began with the traditional three-month training, and then increased in intensity, frequency and duration.

In the last three months, patients ran or bicycled 20-25 miles a week. They were monitored carefully throughout the process.

"The idea is that these patients can gradually increase their level of activity, rather than abruptly terminate it after three months," Ehsani says. "This program is geared to individual needs, since some people can train hard in a short period of time, but others are more limited. Everybody exercises according to his capacity."

Until now,
*there has been no evidence
that exercise can help the
heart itself in patients with
coronary artery disease.*

Patients range from 40 to 65 years old, and vary in the extent of their coronary problems. They cannot be admitted to the program until four months after their heart attack.

Ehsani adds, "Obviously not everybody responds to exercise in the same way. We start our coronary patients at a

low level, basically walking slow and fast and doing low-resistance bicycle work for the first two or three sessions.

"We don't push them. There are no set goals other than to increase the exercise and to adapt very gradually. Actually, it's at least seven months after the heart attack before we can start training most patients fairly vigorously. Cardiovascularly, they may not be able to handle the training, and psychologically, they're not ready for it, especially the people who have never exercised or who haven't exercised for 15 or 20 years. For some of these people, even walking a mile continuously is a major accomplishment."

Ehsani and Holloszy are continuing their studies with coronary patients, but are concentrating now on using a noninvasive test to evaluate the efficiency of the heart during exercise.

To observe heart function, the scientists inject the radioactive chemical technetium into patients with coronary artery disease. The technetium tags red blood cells so that when the heart is scanned, researchers can see an outline of the pool of blood as the heart contracts and relaxes.

"Normally with exercise the ejection fraction — the amount of blood being ejected from the heart — increases," Ehsani says. "In many patients with coronary artery disease, however, the ejection fraction actually decreases with exercise, because a portion of the heart is not getting enough blood. During strenuous exercise, the portion of the heart that's not getting enough blood bulges out in-

stead of contracting normally, because part of the heart is not getting enough oxygen."

Although the Washington University research is conducted with coronary patients, findings are probably most significant for healthy people, Holloszy says.

"Coronary patients are rather limited in what they can do, because we're getting them at the late stages of the disease," he comments. "The point is, if exercise can benefit coronary patients, it's even more likely to have beneficial effects on somebody who has not yet had damage to the heart. Healthy people can start exercising at a much harder level than coronary patients. So I think the preventive aspects of our work are much more important than the therapeutic aspects."

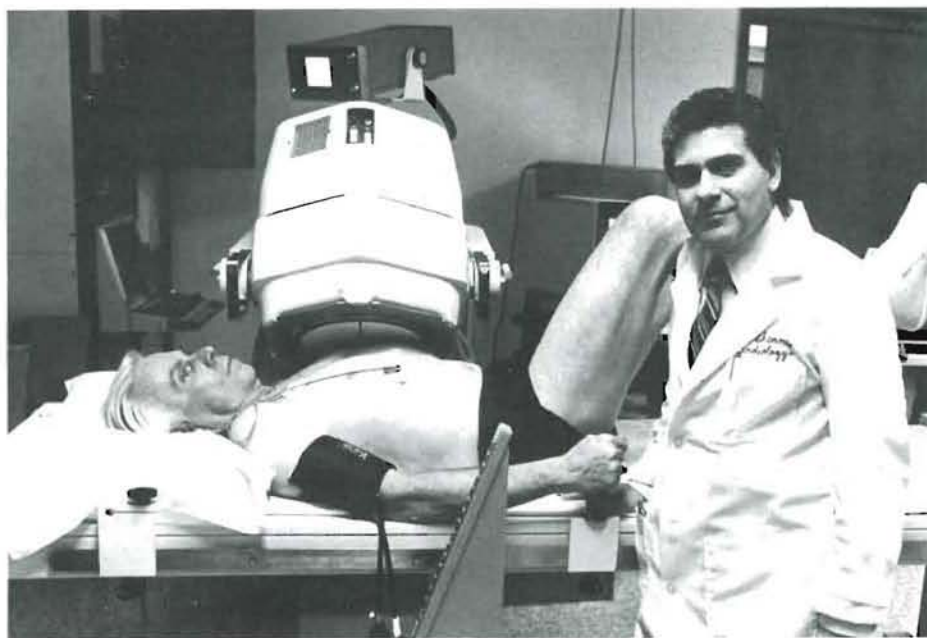
To strengthen the heart and help protect against coronary artery disease, Holloszy says that jogging about 20 miles per week or using an equal amount of energy in other cardiovascular exercise — such as swimming or bicycling — is sufficient.

In a related research project, a team of Washington University exercise physiologists examined the body's adaptation to stress in a group of people just beginning a fitness program. The exercisers reached plateaus in their cardiovascular improvement within three weeks in response to a fixed exercise program. The researchers concluded that to build rather than to maintain fitness, exercise intensity should be increased every three weeks; to avoid injury, however, at least 11 days should be spent at each fitness level.

"It's very difficult to define hard exercise; exercise intensity must be related to a person's maximum capacity. What is hard for one person may be easy for another," Holloszy says. "Exercise that is hard initially may become easy after training. Unless you have an orthopedic or coronary problem, you can run 70 to 80 miles a week without hurting yourself if you have the time and your body has become adapted. However, 20 miles per week is enough for health maintenance." ■



John O. Holloszy, M.D., observes a patient using exercise facilities of the Irene Walter Johnson Institute of Rehabilitation.



Ali A. Ehsani, M.D., conducts a scan to evaluate the heart function of a coronary patient during exercise. For the noninvasive test, scientists inject the radioactive chemical technetium, which tags red blood cells so researchers can observe blood flow as the heart contracts and relaxes.



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SATELLITE IMAGING

by Don Clayton

Helping to Map the Body

The same computer used to create vivid satellite images of Earth is now analyzing complex medical images of the human body. A team of radiologists and engineers has shown that the LANDSAT image-processing computer is able to recognize specific body tissues and realistically color-code them in cross-sectional photographs of the head, chest and abdomen.

Such computer analysis partially resolves a major problem in the promising new field of body scanning known as NMR, nuclear magnetic resonance.

Although NMR images incorporate vast anatomical and physiological information, their extreme complexity makes interpretation difficult. When NMR scans were fed into the LANDSAT computer, it analyzed them just as if they were earthly landscapes and reduced a series of multispectral NMR images into a single, realistic color composite.

This technology-transfer project, a collaborative effort by physicians and engineers from NASA's Kennedy Space Center, University of Florida at Gainesville, and the Mallinckrodt Institute of Radiology at Washington University Medical Center in St. Louis, was presented at the most recent Radiological Society of North America annual meeting, held last November in Chicago.

"What we've done here," says Michael Vannier, M.D., a Washington University radiologist, "is to borrow existing technology already proved successful in analyzing and classifying multispectral satellite images." A former NASA engineer himself, Vannier saw the obvious opportunities for cross-over applications once he realized that NMR images are really quite similar to satellite pictures.

According to Robert Butterfield, the NASA image analysis specialist involved in the project, LANDSAT takes photo-

graphs in several segments of the light spectrum. "That's why we say it's multispectral. For example, when that satellite takes a picture of Chicago or Lake Okeechobee from more than 100 miles out, it takes several photographs — one green, one red, and a couple in the infrared range. Each one is recorded on a separate channel," he explains.

"The amazing thing about this computer program is that it examines all the photos, notes the contrasts among them, eliminates redundancies, combines them into a composite image, and assigns realistic colors to the various components," Butterfield adds.

Like a satellite, the NMR scanner can produce a multitude of pictures with different spectral characteristics.

"And that's precisely what the problem has been with NMR," Vannier adds. "Everyone is asking, 'How do we interpret this data?' At the same slice level in the human body, we receive multiple pictures that have similarities but different contrasts. In applying satellite technology, we've been able to critically examine these contrasts and exploit them to produce realistic composite images. These pictures look real, like you just lifted a slice right out of the human body," says Vannier.

USEFUL COLOR

Color has been used in satellite imaging for a long time, says Douglas Jordan, engineering manager of the Remote Sensing and Image Processing Laboratory at the University of Florida's Institute of Food and Agricultural Sciences. According to the terms of an agreement with NASA, Jordan's Gainesville laboratory houses a LANDSAT image analysis computer. Vannier and Butterfield take the NMR scans there for processing.

Jordan uses the computer more to monitor declining wetlands than encroaching brain tumors. Though the targets are different, the imaging principles are essentially the same.

"The computer-generated colors are selected to make the image look as real as possible, and to enhance the information that was present in all the channels," comments Jordan. "There's a lot we can do to put things in context. For example, soil should be brown, water blue and grassland green. If I assign those colors appropriately, the result is a very pleasant picture. You can appreciate the subtleties that were present in the individual channels."

Appropriate colors for soil and water seem obvious. But the right hues for images of a fluid-filled lung or a tumor mass, for example, are not so simple. Vannier chose colors for the composites very carefully, calling on several other Mallinckrodt radiologists for advice.

"Essentially, our job as radiologists is to extract diagnostic information from an image," says Vannier. "The ability to display the image in color makes that extraction easier. To be as useful as we knew they could be, these images needed to look like fresh-cut anatomic sections. People don't see in just black and white," he continues, referring to the standard appearance of an NMR scan. "Color is our inborn way of handling and understanding multispectral information."

Vannier, the engineers and other physicians he works with have collaborated on more than 30 patient-studies so far, producing color composites for many of them. "But that's not all we've done," he adds. "We've taken the process one step further."

BODY MAPPING

"What we've discovered from analyzing body scans is that, like landscape features, many organs and types of tissue have distinct signatures," says Vannier. A specific "signature" is associated with each component of an image, and enables the computer to separate wheat fields from corn fields, or bone from muscle.

The computer breaks the NMR scan into hundreds of tiny squares and then

Michael Vannier, M.D., seated at the NMR scanner's control console. Vannier has already begun to convert the LANDSAT computer program so that it can operate on the NMR scanner's computer.

searches the image — one square at a time — for any signature the radiologist is interested in. That capacity enables Vannier to create tissue maps of the human body.

"The signatures in NMR scanning are specific and at least as strong, if not stronger, than those that have been used in satellite imaging," adds Vannier. In addition, the LANDSAT computer has artificial intelligence which permits it to learn from its successes and failures. The hundredth body map it creates should be more precise than the first one it processed.

Vannier expects the tissue maps will be particularly useful in two ways. First, they will help radiologists and other physicians see the precise outline of a particular organ or collection of tissues. Second, they should facilitate earlier diagnoses in a wide range of disorders.

"A good example of how the computer can better define an important border is to look at an image of a hematoma, or blood clot, in the brain," says Vannier. "It's very important that the neurologist or neurosurgeon be able to determine the true extent of the hematoma, yet original

NMR scans define its borders poorly.

"By teaching the computer the signature for a blood clot in the brain, we can ask it to show us every part of the image in which that signature can be found. Within a couple of seconds, the computer searches the entire image, coloring any area that has the hematoma signature."

As a result of the search, a tissue theme map is created. The map shows the precise demarcation between the part of the brain containing the hematoma and the parts of the brain that are still unaffected.

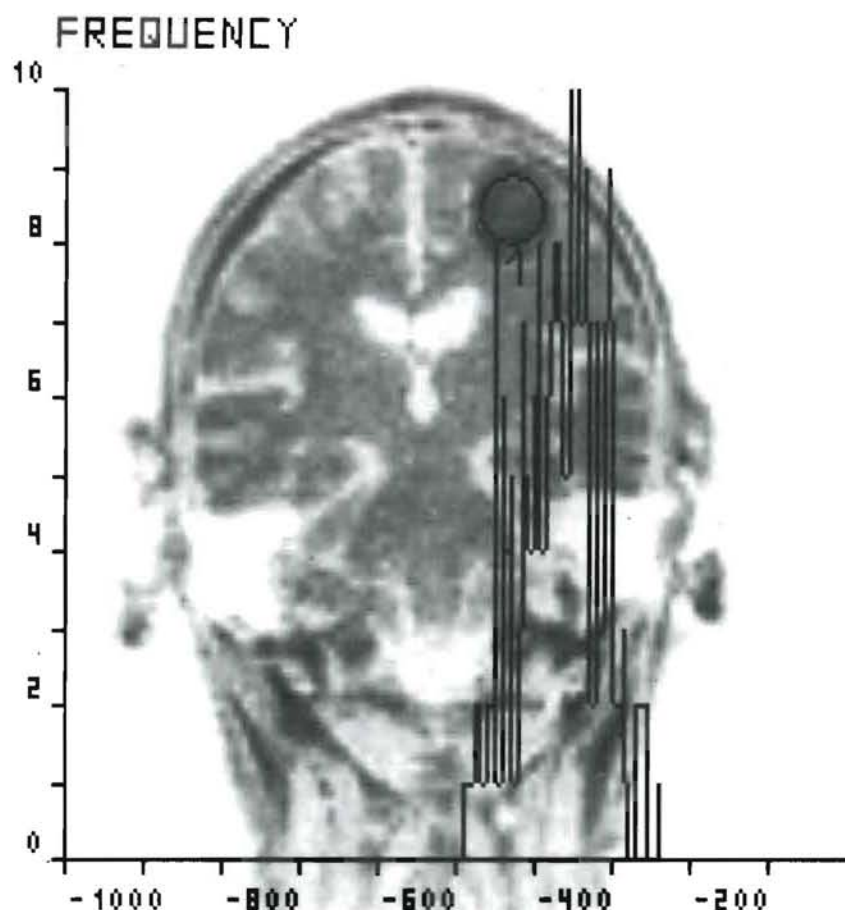
To illustrate how the computer-generated maps might help in early diagnosis, Vannier says, "I can show you images of a patient who has a painful hip, and her other hip feels fine. In the original NMR scan of her pelvis, we could see that the bone of the painful hip was badly deteriorated, but the opposite hip joint looked all clear. We were concerned about the condition of both sides because the particular problem that this woman has usually extends to both hips sooner or later."

When Vannier trained the computer on the deteriorated part of the bad hip, it determined the signature for that type of degeneration. He then ordered the computer to search the entire image for any other locations of that signature and color them.

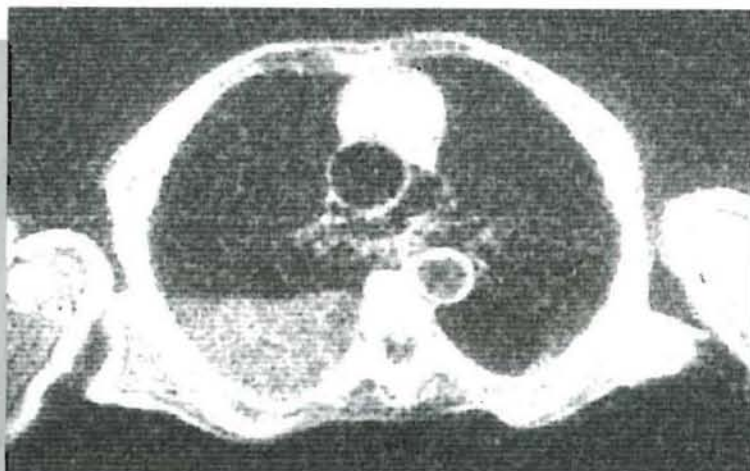
"Sure enough, several spots showed up on the second hip. We would otherwise never have known they were there," says Vannier. "We'll be watching this woman now, to see what happens to the asymptomatic hip. If she does develop pain and abnormality in the same area we've just classified as suspicious, we'll know that we should undertake a much more thorough investigation to see if NMR can be turned into a tool that can permit us to catch this condition early."

PREDICTIONS

During the next few months, Vannier will turn his attention to converting the LANDSAT computer program so that it can operate on the computer that is part



The graph of an NMR signal is superimposed across its correlate image. Subtle changes in the settings of the NMR controls can alter the signal and the contrasts associated with a particular "slice" of the body. A brain tumor is visible at the top-right portion of this image.



of the NMR system. "There is every indication that it should work," he says. "We can't expect everybody to run to a NASA image processing center with their NMR scans. If this technique is to be evaluated in a comprehensive manner, it will have to be converted to a form compatible with NMR computers. Then all NMR centers will have a chance to put it to the test."

Vannier is conservative when he describes what the NMR/LANDSAT marriage has proved so far. But he's confident enough about its impact to venture a few predictions.

"Because each NMR study produces several multidimensional, multispectral images, NMR data will frequently be displayed in a color composite form. Judicious use of color has tremendous advantages for human interpreters," says Vannier.

"Second, some form of satellite image processing will almost certainly be integrated into NMR scanners soon.

"Third, some adaptations of that type of technology will endure. It may be in a much different form than we're using now, but even these first crude experiments show that the potential is very great," says Vannier.

"Satellite imaging has opened a new window into the human body for physicians."

Non-Hodgkins Lymphoma Series

These are three NMR images of the same slice through a patient's chest. Different control settings are responsible for the variations in contrast among the three images. A series of original black and white images like these are selectively combined to create a composite image in which certain contrasts are heightened and redundancies are eliminated. Such composites can later be assigned realistic colors so they are easier to interpret.

EVARTS A. GRAHAM

C E N T E N N I A L S Y M P O S I U M

The School of Medicine and the Mary Culver Department of Surgery hosted the Centennial Symposium for Evarts A. Graham on September 14, 15, and 16, 1983. A total of 314 surgeons who trained under Dr. Graham attended. Included was Dr. Yasuyuki Fukushima from Japan, with his wife, Eleanor. In addition to the speakers shown in the accompanying photographs, there were: Thomas B. Ferguson, M.D., clinical professor of cardiothoracic surgery, who moderated the session on historical perspective and spoke on "Evarts A. Graham, The Man"; Harvey R. Butcher, Jr., M.D., WUMS professor of surgery, who discussed Graham and the education of surgical residents; and Walter F. Ballinger, M.D., WUMS professor of surgery, who moderated the scientific sessions on September 15. Scientific session speakers included: G. Hugh Lawrence, M.D., Ernest A. Sommer Professor of Surgery at St. Vincent's Hospital in Portland, Oregon, "Current Management of Carcinoma of the Lung"; Watts R. Webb, M.D., professor and chairman of the surgery department at Tulane U. School of Medicine, "Energy Without Oxygen"; Hiram C. Polk, Jr., M.D., professor and chairman of surgery at the U. of Louisville in Kentucky, "Host Defense Enhancement: Pursuit of the Holy Grail?"; and Richard M. Peters, M.D., professor of surgery and bioengineering at the U. of California Medical Center, San Diego, "Pulmonary Resection and Gas Exchange."

Scientific sessions on September 16 were moderated by C. Barber Mueller, M.D., emeritus professor of surgery at McMaster University Medical Center, Hamilton, Ontario. Presenters were: Bernard M. Jaffee, M.D., professor and chairman of surgery, SUNY, Downstate Medical Center, "The Endocrine Gut"; Clarence S. Weldon, M.D., professor of cardiothoracic surgery at WUMS, "Surgical Reconstruction of the Outflow Portions of the Right and Left Ventricle"; Maurice M. Jurkiewicz, M.D., professor



Eugene M. Bricker, M.D., '34, presents part of the program at the dinner on September 15. On the screen is a picture of Helen Treadway Graham, professor of pharmacology at WUMS, who married Evarts A. Graham, M.D., in 1916. Bricker also spoke on "Graham and the College of Surgeons," part of the September 15 program, and was instrumental in planning and organizing the centennial symposium. He is clinical professor emeritus of surgery at WUMS.

and chairman of the division of plastic and maxillofacial surgery at Emory U. School of Medicine, "Use of Jejunal Transplants in Patients with Carcinoma of the Cervical Esophagus"; Jessie L. Ternberg, M.D., professor and chief of pediatric surgery at WUMS, "Update in Pediatric Surgery"; Ralph Berg, Jr., M.D., Thoracic and Cardiovascular Surgery in Spokane, Washington, "Coronary Revascularization in Acute Myocardial Infarction"; and the concluding address on future plans by Samuel A. Wells, Jr., M.D., Bixby Professor and chairman of the Mary Culver Department of Surgery at WUMS.

The symposium honored the 100th anniversary of the birth of Evarts A. Graham, and the 50th anniversary of the first one-stage pneumonectomy for carcinoma, which he performed. Graham was chairman of surgery at WUMS and surgeon-in-chief at Barnes Hospital from 1919 until 1957. Scientist, surgeon, teacher and leader, he is often called "The

Father of Chest Surgery." A biography of him, written by Thomas B. Ferguson, M.D., appeared in *Outlook Magazine*, Vol. XVIII, No. 3, Autumn 1981.



Charles L. Eckert, M.D., professor emeritus and Distinguished Professor of Surgery, Albany Medical College of Union University, spoke on "Evarts A. Graham and the American Board of Surgery," which Graham co-founded in 1937.



From left to right are Peter Alch, M.D., of the Uniformed Services University of Health Sciences, William Owens, M.D., and Samuel A. Wells, Jr., M.D., Bixby Professor and chairman of the Mary Culver Department of Surgery, which sponsored the centennial symposium. Wells gave the concluding address of the symposium on September 16, "Future Plans for the Department of Surgery at the Washington University School of Medicine."



Lyman A. Brewer, III, M.D., (left) Distinguished Physician at the Jerry L. Pettis Memorial Veterans Hospital in Loma Linda, California, recounted "The First Pneumonectomy," on the opening day of the symposium. Graham performed the surgery on April 5, 1933. His patient was a 48-year old obstetrician/gynecologist from Pittsburgh. James Gilmore, M.D. With Brewer are Everts A. Graham, Jr., and Mrs. Graham. Graham is former managing editor of the St. Louis Post-Dispatch, and Washington columnist.



Ernst L. Wynder, M.D. '50, and professor emerita Mildred Trotter at one of the social events of the symposium. Wynder, who is founder and president of the American Health Foundation in New York City, discussed the epidemiology of tobacco-related diseases, part of the scientific program on September 15.



Gordon Moore, M.D. '40, John Akin, M.D., and Warren H. Cole, M.D. '20, renew acquaintances. Cole reviewed the development of cholecystography on September 15 at the Everts A. Graham Centennial Symposium.



Standing, from left to right are Lauren Ackerman, M.D., and C. Barber Mueller, M.D. '42, renewing acquaintances with Ada Hanvey, seated and wearing the black jacket. Hanvey was Graham's secretary and administrative assistant for 27 years. Ackerman, professor of pathology at State University of New York, Stony Brook, gave a presentation, "Everts A. Graham—As I Remember Him," in the September 15 program. Mueller, professor emeritus of surgery, McMaster University Medical Center in Hamilton, Ontario, moderated the scientific sessions on September 16.

Samuel Becker Grant,

“Sam Grant was not only an extraordinary man; he was one of the finest physicians and one of the keenest investigators of our generation. The work he did as an undergraduate and house officer put him in a class by himself . . .” So spoke Dr. William Dock, a distinguished physician in his own right, when he learned of Dr. Samuel Grant’s death in November of 1982. He has keen memories of the young physician he learned to respect so highly in the years at the newly organized Peter Bent Brigham Hospital some 60 years ago. Many others who came to know Dr. Grant in later years would agree that he was, indeed, “in a class by himself” for a multitude of reasons.

Drs. Dock and Grant belonged to that fortunate generation of American physicians who were able to apply the fruits of modern medical research to the art of bedside medicine. While William Dock and Sam Grant had known each other as boys attending different high schools in St. Louis, it was at the Brigham Hospital that their friendship was established. Dock well remembers Sam Grant’s decision to go back to St. Louis and open a medical practice as his father had done. He still believes that academic medicine lost a great professor to family tradition. But Sam Grant’s feelings of family loyalty were to result in a career which enriched St. Louis and the Washington University community for more than 60 years.

Visible testimony to the magnitude of his influence on those around him, doctors, patients, and friends, was the crowd which filled Graham Chapel on November 13, 1982, for his memorial service.

A stroke had forced Dr. Grant to retire from medical practice in 1961, but more than 20 years later many people still considered themselves “his” patients. The quality of his character and the style of his medical practice inspired an extraordinary affection in those he knew and cared for; Dr. Grant was not just a physician to them, he was a presence in their lives. Thus, the ceremony in Graham Chapel was not an occasion of sorrow but a cele-

bration of his life and service to the community.

An innately modest man, many of whose achievements were accomplished quietly and behind the scenes, Grant exercised a positive influence as a skilled mediator between the rapidly expanding Washington University Medical Center and the many attending physicians whose work brought them into the affiliated hospitals. And he was an indefatigable supporter of the Medical School and University, using his considerable talents to raise money for student scholarships, housing,

and other institutional needs. Whenever grateful patients would insist on demonstrating their thanks, Grant would try to channel their generosity in the direction of Washington University. The loyalty he inspired continues to benefit two particular entities which bear his name: The Samuel B. Grant University Health Service established in 1963, and the Samuel B. Grant Visiting Professorship and Lecture in Internal Medicine given each year in his honor since 1964. Each is an appropriate tribute to the man whose name they carry. With the Grant Clinic, the group



Dr. Samuel B. Grant.

practice he founded in 1938, they bear witness to his lifelong interest in patient care and clinical research. And they gave Grant enormous pleasure; he attended the Grant Lecture for 20 years after his stroke.

Samuel B. Grant was born on December 10, 1896, the son of a prominent and public-spirited physician, John Mosby Grant. In addition to developing an extensive private practice which was housed in its own medical building, the senior Dr. Grant found time to serve for many years on the St. Louis School Board. His example was certainly an influence on his son's professional career. Sam Grant graduated from Soldan High School, and from Washington University in 1918; he received the M.D. from Washington University in 1920 and spent two years as an intern at Peter Bent Brigham Hospital from 1920 to 1922. During the period from 1917 to 1922, he published no less than eight articles on various aspects of his clinical research, ranging from throat infections to tetany and hyperventilation. His very first article, published in the *Anatomical Record* of 1917, grew out of his observation of an anomaly in a cat's vascular system during a course in comparative anatomy in the Zoology Department. This undergraduate effort was early evidence of his unusual intellectual curiosity and diligence. A 1920 paper entitled "A Study of Forced Respiration: Experimental Production of Tetany" was published from the Physiology Department of Washington University; the co-authors, Grant and Dr. Alfred Goldman, acknowledged the "kindly interest" of three faculty members, Dr. Joseph Erlanger, Dr. Philip Shaffer, and Dr. W. McKim Marriott. In a series of experiments they established the fact that "all the essential symptoms of tetany could be produced in the human subject by forced respiration." The human subjects in this series of experiments (one of which induced a full convulsion) were the authors themselves. This risky style of experimentation was not unusual at this time. Another outstanding series

of experiments on the etiology of acute inflammations of the nose, pharynx and tonsils, was performed in the Pathology Department at Washington University. One of the co-authors of this article, Dr. Stuart Mudd, submitted an original version of this work as a dissertation to Harvard University where it was awarded the Boylston Medical Prize, given each year since 1826 for outstanding research.

By the time young Dr. Grant had completed his training and was applying for his first academic position as an instructor in the Department of Medicine at Washington University in 1924, he was able to list 17 publications in a variety of medical



A pre-medical portrait of the physician as a young St. Louisan.

and scientific journals to his credit. This record was an unusual one in a physician whose intention had always been to enter private practice; it reflected Sam Grant's special combination of curiosity, competence, and drive.

In addition to his firm grounding in clinical research and bedside medicine, Grant returned to St. Louis in 1924 with the affection of a vivacious young Bostonian who had trained as a nurse while he was a house officer at Peter Bent Brigham. Natalie Neville became his wife in

1926, and brought to their partnership her own expertise in nursing and occupational therapy, as well as a special "joie de vivre" that was infectious in the best sense of that word. Grant started out in private practice with several colleagues on Sarah and Olive, and later worked in the Beaumont Medical Building. As his practice expanded, the idea of having his own group practice of internists housed in an autonomous building grew in his imagination. It was, in fact, not an entirely new idea, but a family tradition; his father had owned a building, but had always practiced alone. The first group practice in the United States was founded by the Mayo brothers in 1887; the Middle West was the region in which this pattern of practice was most common, but while the idea would gradually take hold, it was still a risky business in 1938, particularly when it involved the use of a new building especially constructed for that purpose. Sam Grant was not afraid of taking a chance on his idea.

Mrs. Grant now freely admits that this was one time when her belief in her husband's judgment wavered. To make such an investment, during a decade of national depression and at a time when there were three young Grants to raise, seemed a dangerous proposition — so much so that she remembers others dubbing the proposed building "Grant's Tomb." Sam Grant's vision of a new building designed for his group practice called for the services of an architect, and he chose the architect on the basis of his own instinct for excellence. He saw a doctor's building in Clayton which appealed to him and found that Harris Armstrong was the man he wanted for the proposed Grant Clinic. He contacted Armstrong, and these two men in different professions began a collaborative process which resulted in the Grant Clinic Building at 114 North Taylor Avenue. It was finished in 1938. That it is still refreshing to the eye in 1983 is in large part due to the courageous vision of both men.

Sam Grant and Harris Armstrong approached the problem of the new clinic's architecture as partners in an exciting enterprise. The architect spent hours in Grant's office watching how examining room space was used. Their goal was to produce a building efficient to use as well as pleasant to inhabit. The boredom so often associated with waiting for a doc-



The Grant Clinic in 1938. It was designed by prominent architect Harris Armstrong, and described by Frank Lloyd Wright as one of two interesting buildings in St. Louis.

tor's appointment was avoided in a variety of ways. There was a small garden just inside the entrance; the rooms were sunny and cheerful, and a fireplace was included as part of the warm interior decor. Mrs. Grant helped the architect select furniture and suggested that each examining room have a wooden tray with puzzles to pass the time. Like the building itself, the simplicity and warmth of the interior has endured.

Mrs. Grant recalls that there was some concern in 1938 that such a modern building would not "sit well" in a neighborhood with so many houses from an earlier era. In time such concern proved unnecessary, and as the years have passed, the Grant Clinic with its soft handmade bricks from southern Missouri has be-

come a distinguished landmark of Central West End architecture. Indeed, Frank Lloyd Wright once remarked on a visit to St. Louis that the two most interesting buildings in town were Union Station and the Grant Clinic.

The Clinic was featured in the *Architectural Record* of September 1939 as a "Physician's Office Designed for Control from a Central Point." As this title indicates, functionalism was then the reigning style in American architecture. The Grant Clinic showed, and shows, that functionalism and rationality do not have to produce a cold or mechanistic building. Three additions have been made to the original structure, but they have kept to the spirit and intention of the original building. For patients and staff, the Grant Clinic building continues to be a pleasure; to the passerby, it is still astonishingly fresh in conception. Sam Grant's building avoids the banality so commonly seen in medical office architecture and remains true to his original vision of humane medical practice in a human setting. He and his associates later added a kitchen and lunchroom to the building, and patients were able to have simple refreshments provided, particularly after x-ray examinations.

The drive and organizational ability it took to establish his clinic and expand its practice meant that Grant had less time for the research he had once enjoyed so much. Nonetheless, he maintained his membership in such professional groups as the Central Interurban Clinical Club. This was an elite group of 109 prominent internists from the Middle West, 40 of whom were deans or chairmen of departments of medicine. He was also a member of AOA, the Society of Sigma Xi, a Diplomate of the American Board of Internal Medicine, and a Fellow of the American College of Physicians. Though Grant's professional and social life were demanding, and he was a devoted family man, he still managed to find time to serve Washington University. Among his extracurricular activities were spearheading the fund drive for the Spencer Olin Medical Stu-

dent Dormitory, serving as a member of the University's Board of Directors, and working to obtain additional scholarship funds for the medical school.

Despite his accomplishments, at least one patient had the temerity to criticize his financial acumen. When Grant made a housecall, this patient asked if he would examine his wife and another relative who was sick upstairs. Grant sent a bill for one housecall, but by return mail came a check for three times that sum with a note from the patient advising the physician that although he had great faith in his medical skill he was obviously "a lousy businessman." Another patient recalled his ability to deal wisely with the psychosocial causes of illness. A victim of migraine headaches, she was given appropriate medication; in addition Dr. Grant advised her how to find a less stressful living situation. The dual therapy was successful.

With his responsibilities as attending physician, clinical professor, and chief executive of a group practice, Grant still found time to relax. His friends and fam-



Grant and friends at his DeSoto farm. In the front are Dr. Harry Alexander and Towner Phelan. In the back, Grant and former psychiatry department head Dr. Edwin Gildea.

ily remember the joy he always took in his farm located in DeSoto, Missouri, near the Big River. This 120-year-old log cabin was the site of countless happy occasions shared with friends, colleagues and house staff. Piano music provided by Grant, and his wife's homecooking, were special attractions. A mixture of friends (medical, scientific, and otherwise) reflected the Grants' easy and unpretentious sociability. Whether their background was in biochemistry or banking, guests knew that a weekend in DeSoto meant a relaxed and relaxing time. Torrential rains some weekends made the nearby river rise to such an extent that one guest (who happened to be a Nobel Laureate) missed giving an important lecture. It seemed a small price to pay for such generous hospitality.

Grant's sons remember their father working hard on the farm, but that in itself was a form of unwinding. He put his efforts into building furniture, studying soil or crops, and even managed a small herd of Herefords. Swinging a scythe and chopping stumps were strenuous exercise, but the demands were different from those Dr. Grant faced in medicine. He never mentioned the pressures of his practice on the farm. And he was always sure to begin fishing on the very day the season opened, often with his friend Dr. Warren Cole.

By 1961 the Grant Clinic had become a model of group practice. But its unique quality, its architectural integrity and its organizational character were products of Sam Grant's imagination and character. His personality was its foundation. So when Dr. Grant suffered a stroke that year, there was reason to fear for the future of his enterprise. Despite the blow of his illness and the westward move of many other physicians, the Grant Clinic has endured. Like the building which houses it, the clinic has changed with time but has kept its original strengths intact. Two of Dr. Grant's sons, John and Neville, are members of the staff. His third son, Sam Jr., is chairman of the Department of History at Southern Illinois



Dr. Grant responds to a friend's greeting at the dedication of the Samuel B. Grant Student Health Center. Then-chancellor Thomas Eliot looks on.

University in Edwardsville.

In the years before 1961, Grant had been an exemplar as a physician; he continued to be an exemplar after his retirement from practice. Though his mobility and vocabulary were limited by his stroke, his courage and humor were undimmed. All Mrs. Grant's energy and ingenuity, as well as her early training in nursing and occupational therapy, went into making her husband's recovery as full as possible. With her help he learned to write, to weave, and to play the piano again. And he walked every day, regard-

less of the weather. Rails were constructed inside and outside of his house so that he could accomplish his walking "rounds." Despite his impairment, Grant made any visitor feel grateful for his company; he was always responsive and welcoming to guests of all ages.

The Reverend William Chapman spoke for all his friends and colleagues in Graham Chapel on November 13, 1982, when he expressed gratitude "for the companionship and example of one who walked with strength and then waited with grace . . ."

Newsbriefs

Gift Establishes New Neuroscience Center

The James S. McDonnell Foundation has provided a \$5 million gift to establish the Center for Cellular and Molecular Neurobiology at the School of Medicine. The announcement was made by Chancellor William H. Danforth, M.D. This gift also assists the ALLIANCE FOR WASHINGTON UNIVERSITY in achieving its \$300 million goal.

According to Gerald D. Fischbach, M.D., head of anatomy and neurobiology and director of the new

center, the \$5 million gift will be used over a five-year period. Research areas will include the basis of electrical and chemical excitability of neurons, as well as investigations on the development, growth and survival of nerve cells. The center will also support research on neurotransmitters and electron microscopic study of nerve cell ultrastructure.

"The new neurobiology center joins the McDonnell Center for Studies of Higher Brain Function at the School

of Medicine, established in 1980 with a \$5.5 million gift from the McDonnell Foundation. The efforts of researchers at both centers will continue to enhance the School of Medicine's preeminence in basic and clinical neuroscience research and expand our understanding of the nervous system and brain," says Samuel B. Guze, M.D., vice chancellor for medical affairs and president of the Washington University Medical Center. ■



Pierce to Hold First Seldin Professorship

The family of the late Herman Seldin has pledged \$1 million over the next four years to establish the Selma and Herman Seldin Professorship of Medicine in Pulmonary Diseases at the School of Medicine. John A. Pierce, M.D., has been appointed to hold the first professorship.

Pierce is an internationally recognized authority on the development of emphysema. Chief of the pulmonary disease division of the Department of Medicine, Pierce also holds appointments as physician at Barnes and Children's Hospitals at the Washington University Medical Center.

Pierce's research has focused on lung biochemistry and emphysema, a disabling disease characterized by deformity of the connective tissue framework of the lung. Pierce's measurements of

collagen and elastin (the major connective tissue proteins in the lung) pioneered the modern era of lung research. Pierce and his colleagues, Robert M. Senior, M.D., professor of medicine, and Charles Kuhn, M.D., professor of pathology, produced an experimental model of emphysema that is the basis for the current theory of emphysema development.

Pierce joined the faculty at Washington University in 1967, when he was appointed associate professor of medicine, chief of the pulmonary division of the Department of Medicine and chief of the pulmonary disease division of John Cochran Veterans Administration Hospital. He was named professor of medicine in 1972.

Pierce received the doctor of medicine degree from

the University of Arkansas School of Medicine. He served an internship and residency in the U.S. Public Health Service. Before coming here, Pierce was Professor of Medicine at the University of Arkansas Medical Center in Little Rock.

A diplomate of the Ameri-

can Board of Internal Medicine, Pierce is also a fellow of the American College of Physicians and the American College of Chest Physicians. His extensive professional service has included a consultancy to the National Heart, Lung and Blood Institute. ■



Mrs. Selma Seldin is joined by Samuel B. Guze, M.D. (left), and John A. Pierce, M.D. (right), at the announcement ceremony establishing the Seldin Professorship.

WU Faculty Members Awarded Horwitz Prize

Viktor Hamburger, Ph.D., Rita Levi-Montalcini, M.D., and Stanley Cohen, M.D., have been awarded Columbia University's Louisa Gross Horwitz Prize for 1983. This prize, awarded annually since 1967, is bestowed upon outstanding researchers in biology or biochemistry and often precedes the Nobel Prize.

Hamburger is Edward Mallinckrodt Distinguished University Professor Emeritus of Biology, and Levi-Montalcini is professor emerita of biology. Cohen left Washington University in 1959 for Vanderbilt University.

Their collaboration at Washington University in the late 1940s and early 1950s culminated in the discovery of nerve growth factor (NGF). They found that



smooth muscle cells innervated by sympathetic neurons secrete this protein. Growth and maintenance of sympathetic nerve terminals innervating involuntary muscle depend on the muscle cells' acquisition of this molecular agent. Sympathetic nerve cell terminals absorb NGF and carry it back to their cell



bodies, thus ensuring the nerve cells' survival.

Subsequently, Hamburger and Levi-Montalcini demonstrated that outgrowing nerve fibers can sense chemical signals such as NGF over considerable distances, following them to the fibers' appropriate destinations. Cohen's early work with NGF helped lead

to his discovery of Epidermal Growth Factor (EGF), which regulates growth and differentiation of many types of cells. The study of EGF's mechanism of action paved the way for elucidating the mode of action of products of carcinogenic viruses.

The discovery and study of NGF laid the groundwork for much of our present understanding of how nerve fibers make connections, as well as our understanding of how other cell types grow and differentiate.

Hamburger and Levi-Montalcini have received several awards, including honorary doctor of science degrees from Washington University, as well as Founders Day Distinguished Faculty Awards. ■

New Faculty Member Joins the Medical School

J. Regan Thomas, M.D., has been appointed assistant professor of otolaryngology at Washington University School of Medicine. Thomas's appointment was announced by John M. Fredrickson, M.D., professor and head of the Department of Otolaryngology.

Thomas is also on staff at Barnes and Jewish hospitals at the Washington University Medical Center. Before joining the Washington University faculty, he was assistant professor of otolaryngological surgery at the University of Missouri Medical Center.



A recipient of the bachelor of arts degree from Drury College in 1968 and the doctor of medicine degree from

the University of Missouri School of Medicine in 1972, Thomas completed a residency in surgery at Yale University and a residency in otolaryngology at the University of Missouri School of Medicine. He also served a fellowship in facial plastic surgery that was cosponsored by the American Academy of Facial Plastic and Reconstructive Surgery, Inc., and M. Eugene Tardy, M.D.

Thomas is a member of several organizations and committees, including the American Board of Otolaryngology, the American College

of Surgeons, the American Academy of Otolaryngology — Head and Neck Surgery, and the American Academy of Facial Plastic and Reconstructive Surgery.

He has received the American Medical Association's Physicians Recognition Award, and serves on the board of directors of the Missouri Ear, Nose and Throat Society. Thomas is also a member of the medical school admission committee at Washington University. ■

Newsbriefs

Symposium in Honor of Retiring Department Head

Members of the Department of Physiology and Biophysics organized an international symposium to mark the retirement of Carlton Cuyler Hunt, M.D., Edward Mallinckrodt, Jr., Professor and department head. The symposium was held September 23; Hunt's retirement as department head was effective September 30. Eleven distinguished physiologists and biophysicists from throughout the United States, and from France and Japan, participated. Eight were former colleagues of Hunt's, from physiology departments he had chaired earlier in his distinguished career. They now chair physiology departments from Kyoto to Colorado to Connecticut.

Hunt and his wife, Marion (a frequent contributor to

Outlook Magazine), will reside in Paris, France, where he will continue his research in the sensory innervation of muscles, under the auspices of the College de France.

Hunt has been head of the Department of Physiology and Biophysics at Washington University School of Medicine since 1967. During his 16 years as department head, he has built an internationally recognized department that is strong in biophysics and cell biology, as well as in neurophysiology. Before joining the faculty of Washington University, he spent three years at Yale University, where he initiated a revitalization of the department of physiology.

From 1957 to 1964, Hunt chaired the physiology department of the University of Utah School of Medicine,

attracting top scientists and developing one of America's most productive and influential neurophysiology research groups. Hunt's career also included positions at Albert Einstein College of Medicine, where he conducted advanced studies of muscle spindles and their influences on spinal reflexes; the Rockefeller Institute for Medical Research; and Johns Hopkins University, where he was able to describe, for the first time, the efferent innervation of muscles in mammals. Hunt received the M.D. degree from Cornell University Medical School in 1942. ■



Dr. Motoy Kuno (left), professor and chairman of the physiology department, Kyoto University Faculty of Medicine, chats with Carlton Hunt, M.D. (right), the symposium's honoree.



Drs. Edward Perl, a speaker, and Sherman Beacham, an attendee, exchange ideas during a break. Perl is professor and head of the Department of Physiology at the University of North Carolina School of Medicine; his topic was "A Nociceptive Story from One End of the Neuron to the Other," and was the concluding session of the symposium.



In the lobby of the McDonnell Medical Sciences Building are Drs. A. Robert Martin, Yves La Porte, and Guillermo Pilar. Martin, professor and chairman of physiology at the U. of Colorado Medical Center, spoke on "Post-synaptic Chloride Channels in the Central Nervous System." La Porte is the administrator of the College of France and president of the Assembly of Professors. His presentation at the symposium was "Recent Observations on the Dynamic Fusimotor System of Cat Spindles." La Porte was a post-doctoral fellow at Washington U. in 1945, studying under professor George Bishop. He heads the college where Hunt will continue long-term research. Pilar is professor and head of the physiology section at the U. of Connecticut. His topic of discussion was "The Influence of Muscle on Cholinergic Development."

Full Agenda of Fall Lectureships

The fourth S. Richard Silverman Lectureship in Hearing and Deafness, sponsored by the Central Institute for the Deaf, was delivered by Peter MacNeilage, Ph.D., professor of linguistics and psychology at the University of Texas. MacNeilage, an expert on speech production, is director of the Phonetics Laboratory at the University of Texas. He discussed the

planning and production of speech.

The first annual Edward Massie Lecture in Cardiovascular Disease, sponsored by the cardiology division, was delivered by Bernard Lown, M.D., professor of cardiology and director of the Cardiovascular Research Laboratory at Harvard University School of Public Health. President of the International

Physicians for the Prevention of Nuclear War, Lown's talk centered on the physician's role in confronting the threat of nuclear war.

Yuet Wai Kan, M.D., head of the Division of Genetics and Molecular Hematology at the University of California (San Francisco), presented the 11th annual Carl V. Moore Lecture at the School of Medicine. Sponsored each year

by the Department of Medicine, the Moore Lecture honors Carl V. Moore, M.D., the first vice chancellor for medical affairs at the School of Medicine and a former president of the Washington University Medical Center.

Kan discussed the role of recombinant DNA in the diagnosis and treatment of hemoglobin disorders.

(continued next page)

EB Center Established

A multidisciplinary center for research and treatment of the rare genetic skin disease, epidermolysis bullosa (EB), has been established at Washington University School of Medicine. The center was created by a \$25,000 donation from the Dystrophic Epidermolysis Bullosa Research Association (D.E.B.R.A.), a national organization of patients, families and others concerned about the disease.

EB is a rare skin disease affecting 25,000 to 50,000 children in the U.S. Blistering, scarring and destruction of the skin and mucous membranes of the gastrointestinal, urinary and respiratory tracts are symptoms of EB, which is actually a group of 14 disease varieties.

Because the disease is so rare, there are few places where those afflicted with EB can seek treatment; commonly, EB patients have traveled extensively, seeking

unproven (and costly) cures.

Patients at the Washington University EB center are admitted to the School of Medicine's Clinical Research Center or to Children's Hospital at Washington University Medical Center. A team of physicians and other health care personnel focus on preventing the serious effects of EB, such as infection, scarring, loss of movement in the major and minor joints, blood and protein loss through the skin, gastrointestinal scarring, eye problems and chronic malnutrition.

According to Eugene A. Bauer, M.D., professor of dermatology at Washington University, the center will provide patient care and conduct basic research on the cause of EB. By performing biochemical tissue tests to distinguish among the forms of EB, researchers may one day be able to devise specific therapy for EB patients. ■

FURTHERMORE



Virginia V. Weldon, M.D., deputy vice chancellor for medical affairs at the School of Medicine, has been named chairman-elect of the Council of Academic Societies of the Association of American Medical Colleges (AAMC). Through the council, medical college faculty members participate in governing the AAMC. The AAMC represents the entire community of academic medicine, including medical schools and students, teaching hospitals and biomedical societies from throughout the U.S. The Council of Academic Societies, composed

of 73 academic and scientific societies in the biomedical field, has an active membership estimated at 100,000.

Weldon, a representative to the Council of Academic Societies since 1976, is vice president of the Washington University Medical Center and professor of pediatrics at the School of Medicine. A staff member at Barnes and Children's hospitals at the medical center, she is a specialist in pediatric endocrinology, with special interest in the mechanisms of abnormal growth in childhood.

Weldon came to the university in 1968 as an instructor and was named professor of pediatrics in 1979. During her career at the medical school, she has served as assistant to the vice chancellor for medical affairs, assistant director of the Clinical Research Center, and co-director of the Division of Pediatric Endocrinology and Metabolism.

Newsbriefs

Her professional memberships include the Endocrine Society, Society for Pediatric Research, Lawson Wilkins Pediatric Endocrine Society, the American Academy of Pediatrics, the American Association for the Advancement of Science and the St. Louis Medical Society. She has served as a government consultant on several projects, most recently as chairman of the General Clinical Research Centers Advisory Committee of the National Institutes of Health. Currently a member of the National Advisory Research Resources Council of the National Institutes of Health, she has also been elected to the Institute of Medicine of the National Academy of Sciences.

A number of awards and honors have been bestowed on Weldon, and she is the author of many journal articles on pediatric endocrinology. A member of the board of directors of the United Way of Greater St. Louis and the Center Trust Company of St. Louis, she is also a commissioner of the St. Louis Zoological Park.

John M. Fredrickson, M.D., head of the Department of Otolaryngology at the School of Medicine, has recently been named as second Lindburg Professor of Otolaryngology by William H. Danforth, M.D., chancellor of Washington University.

This endowed professorship in otolaryngology was established in 1966 by the late Arthur R. Lindburg, president of Lindburg Enterprises, in appreciation of the

dedicated care he received from the Department of Otolaryngology.

At Washington University Medical Center, Fredrickson is otolaryngologist-in-chief at Barnes and Children's hospitals; he is also consultant to Jewish Hospital.

Richard V. Bradley, M.D., has been re-elected a member of the Executive Faculty of Washington University School of Medicine in St. Louis.

Bradley was elected by the school's part-time faculty to serve on the council, which is the school's governing body. He represented the part-time faculty for the 1982-83 term.

A 1952 graduate of Washington University School of Medicine, Bradley interned and served his residency at the Barnes Hospital. He joined the academic staff of the School of Medicine in 1968 and became an assistant professor of clinical surgery in 1974. He is also a member of the staff of the Barnes Hospital and the St. Louis Children's Hospital, and is past president of the Barnes Hospital Society.

Bradley is a member of the American College of Surgeons, the Southern Medical Association and the Missouri State Medical Association. He is a past president of the Missouri State Medical Association and the St. Louis Medical Society.

Lee N. Robins, Ph.D., professor of sociology in psychiatry, has received the 1983 Distinguished Leadership

Award from the Mount Holyoke Club of St. Louis. The award was presented at a public lecture in Robins' honor by M. Elizabeth Tidball, Ph.D., professor of physiology at George Washington University Medical Center. Established by St. Louis area alumnae of Mount Holyoke College to recognize women who have made outstanding contributions in their fields or who have consistently upheld the highest professional standards, the award cannot be given to a Mount Holyoke graduate.

Robins, a professor of sociology in psychiatry at Washington University School of Medicine since 1968, has been a leader in follow-up studies of children, in studies of drug use by returning veterans, and in the development of instruments for assessing mental disorders in the general population. Currently a principal investigator of the Epidemiological Catchment Area project, which is a study of drug use by returning veterans, she is also an investigator working on the MacArthur Network on Risk and Protective Factors in the Major Mental Disorders. She also directs a training program in psychiatric epidemiology and biostatistics.

Robins holds bachelor's, master's and doctoral degrees from Radcliffe College in Cambridge, Massachusetts. She serves on a number of editorial boards, and is a member of many advisory committees and professional organizations. She is a member of Phi Beta Kappa

and Sigma Xi. Robins has received the National Institute of Drug Abuse Pacesetter Research Award, the American Psychopathological Association's Paul Hoch Award, the American Public Health Association's Rema Lapouse Award, and the Radcliffe College Graduate Society Medal Award.

Lectureships (continued from page 19)

Steven Muller, Ph.D., president of the Johns Hopkins University, delivered the inaugural Henry G. Schwartz Lectureship at Washington University School of Medicine. Muller's lecture was entitled "The Post-Gutenberg University." This lectureship was created by former residents and colleagues to honor Henry G. Schwartz, M.D., August A. Busch Jr. Professor of Neurological Surgery at the School of Medicine. Speakers for the Schwartz lectures will represent various disciplines reflecting Schwartz's interests: education; human affairs; neurological surgery and the neurosciences.

Schwartz received the 1983 Award of Merit from the St. Louis Metropolitan Medical Society. His other awards and honors include the Johns Hopkins Heritage Award, the Distinguished Service Award of the Society of Neurological Surgeons, and the Harvey Cushing Medal of the American Association of Neurological Surgeons. Schwartz is in the archives of the Leaders in American Medicine.

The Alumni REPORT

Alumni Say Yes to Phonathoners



Medical Eliot Society Chairman, Marvin Levin, M.D. '51, (left) kicks off the evening of calling with a pep talk for volunteers. Among the thirteen volunteers who called their classmates for support of the School of Medicine were: (clockwise) Phonathon Programs Chairman Robert Burstein, M.D. '48; John Davidson, M.D. '52; Virgil Loeb, M.D. '44; Llewellyn Sale, M.D. '40; C. Read Boles, M.D. '43, and George Koehler, M.D. '58.



Paul Hagemann, M.D. '34, and Stanley Hampton, M.D. '34, called their classmates to discuss a planned 50-year reunion class gift. Virgil Loeb, M.D. '44, is leading a similar program for his 40-year reunion class.



Medical Annual Programs Chairman Robert Drews, M.D. '55, congratulates phonathoner Meredith Payne, M.D. '50. Payne won a bottle of wine for being one of the star callers of the evening.

CLASS NOTES

'50s

Joseph V. Sharrotta, M.D. '50, an internist, was recently honored by Marymount Hospital in Cleveland, Ohio, for 25 years of service. Sharrotta joined the Marymount staff in 1958 after completing his training at St. Vincent Charity Hospital and Cleveland Clinic.

James B. McClenahan, M.D. '57, former director of the Student Health Center at Stanford University, has been appointed public health officer for Amador County, California.

Gerald E. Hanks, M.D. '59, has been elected president of the American Society for Therapeutic Radiology and Oncology. Hanks is currently associate clinical professor of radiology, University of California at Davis, and director of the Radiation Oncology Center, Sacramento.

'70s

Edward F. Hill, M.D. '73, has joined the medical staff at East Carolina University's School of Medicine as an assistant clinical professor of family medicine. From 1976 to 1983, Hill was in private practice with Group Health Cooperative of Puget Sound in Olympia, Washington.

Michael Deldin, M.D. '75, a pediatrician who has been in private practice in Los Banos, California, since 1981, is now completing con-

struction of a new office in that town.

Charles G. Newton, Jr. M.D. '75, has joined the heart surgery team of Bridgeport Hospital in Connecticut. Newton was, most recently, an associate staff surgeon at the Cleveland Clinic.

Timothy Fete, M.D. '77, has joined the Colorado Springs Medical Center in Colorado Springs, Colorado.

Norman L. Foster, M.D. '77, recently returned to his hometown to receive the "Young Alumnus of the Year" award from MacMurray College in Jacksonville, Illinois. Foster is a neurologist currently completing a three-year residency at University Hospital in Salt Lake City.

Major Kurt K. Kroenke, M.D. '77, has been assigned to Brooke Army Medical Center in San Antonio, Texas, as an internist in the department of medicine. Kroenke was previously with Martin Army Hospital at Fort Benning, Georgia.

'80s

Brian E. Laux, M.D. '80, has become director of emergency medicine at Clifton Springs Hospital and Clinic in New York.

Terence Mealman, M.D. '82, recently began family practice at the Rural Family Practice Clinic in Reinbeck, Iowa. Before moving to Iowa, Mealman completed a residency program at St. Luke's Hospital in Kansas City.

Former House Staff

Laurie D. Ervin-Mulvey, M.D., recently completed a fellowship in pediatric ophthalmology at Wills Eye Hospital in Philadelphia.

Ervin-Mulvey has moved to Princeton, New Jersey, where she has joined Eye Physicians and Surgeons group practice.

Patrick King, M.D., is the newest member of Willcockson Associates in Yanktown, South Dakota. He completed an internal medicine residency at Jewish Hospital and an ophthalmology residency at Barnes Hospital.

Dale R. Pokorney, M.D., a former dermatology resident at Barnes Hospital, has joined the staff of Sharon General Hospital in Sharon, Pennsylvania.

Kenneth L. Roark, M.D., recently opened the MED-ONE Medical Center in Norton, Virginia. Roark most recently served as an emergency medicine practitioner for National Emergency Services.

Erratum

On page 17 of the Summer 1983 issue, the picture labelled as Stanley Lang, Ph.D., is actually a photograph of Kenneth J. Bennett, M.D., assistant clinical professor of surgery.

Bennett was the 1983 recipient of the Sydney S. Pearl Award for inspirational teaching. Our apologies to Stanley Lang and Ken Bennett for the error.

In Memoriam

R. Robert Bates, M.D. '46, died June 4, 1983, of liver cancer. In family practice for 34 years, Bates lived in Tucson for 48 years. His daughter Theresa Bates Ananda, one of Bates's eight children, is a 1978 graduate of the Occupational Therapy School at WU. She informed OUTLOOK of her father's death. Surely echoing the feelings of other children whose parents were dedicated medical practitioners, she writes: "(During my childhood) he didn't spend much time with us because he was always working. Ever since I can remember, he'd wake up at 5:00 a.m. for hospital rounds. Then he would spend ten hours at the office with patients, and after supper he would call them to find out how they were doing. On his day off and on weekends, he made house calls and nursing home visits. He spent his vacations going to medical seminars and reading journals. As a child, I did not understand this nor really know what he was doing, until his death."

Ms. Ananda says that her father "attributed his medical knowledge and skills to Washington U. Medical School, often saying that 'it is one of the best medical schools in the country.'" For over 17 years, Bates was a member of the Century Club.

After interning at San Joaquin General Hospital in Stockton, California, Bates took a residency at St. Mary's Hospital in Tucson and at

St. Joseph's Mercy Hospital in Detroit. He began his family and geriatric medical practice in Tucson in 1949, serving as a staff physician at all Tucson hospitals. In 1953, Bates spent two years with the U.S. Army Medical Corps at Fort MacArthur, California.

Memorial contributions may be made to Casa de los Ninos Crisis Nursery in Tucson, or the Newman Catholic Student Center at the University of Arizona.

Grandison Royston, M.D. '07, died June 23, 1983, at a hospital in Little Rock, Arkansas, following a brief illness. Royston was the obstetrician who delivered the first baby ever born at St. Louis Maternity Hospital in 1927.

A native of Washington, Arkansas, Royston studied in Vienna, Berlin and Tübingen, Germany, following graduation. He was appointed assistant in obstetrician/gynecology at WUMS and Barnes Hospital in 1921 and was named emeritus in 1953. During a career spanning 35 years, Royston delivered over 8300 infants.

Roy W. Robinson, M.D. '25, died at Price, Utah, on June 15, 1983, at age 82. His brother, Frank H. Robinson '35, notified OUTLOOK and noted that his brother was still in part-time practice, only entering the hospital one day before his death, and then only at the insistence of his office nurse.

Ernie Simms died suddenly on September 11, 1983. As a young man of 19, he had

begun work at Washington University 47 years ago as a laboratory technician in the department of surgery. By the start of World War II, he had worked in clinical laboratories at Jewish Hospital and Homer G. Phillips.

Once he returned from military service, Washington University was his permanent home. In 1953, he joined the laboratory of Arthur Kornberg in the department of microbiology. During the next six years, he was part of an exceptional research team in Kornberg's laboratory, consisting of Maurice Bessman, Julius Adler, Robert Lehman, and Kornberg. Very quickly, his abilities made him a full partner in the research effort, despite the fact that he had a very limited formal education: Ernie had only two years of college training. He co-authored seventeen scientific publications describing the group's pioneering research on DNA, research that was to lead in 1959 to the awarding of the Nobel Prize to Arthur Kornberg, the group's leader. In accepting this award, Kornberg emphasized the group's team effort, naming Ernie as a key contributor.

Paul Berg, a recent Nobel Laureate, writes: "I first met Ernie when I came to Washington University in 1953 to do postdoctoral work with Arthur Kornberg. I still remember how astonished I was at how rapidly and efficiently he learned the language, skills and sophistication of biochemistry and microbiology. Before long, he outgrew the 'technician' status and

became an important contributing member of the Kornberg 'group.' He was regarded by all as an equal, in all phases of the projects, technically and intellectually. When Ernie said something about an experiment, you could count on it and more often than not his intuition was as infallible as his experiments."

When Kornberg's research team left for Stanford, Ernie stayed and joined the laboratory of Herman Eisen, new department chairman. Eisen was interested in the chemistry of antibody molecules, and Ernie's experience was perfect for this new effort. Very quickly, he became an accomplished researcher in immunology and, over the course of 15 years, published several papers.

In addition to his talent as a researcher, Ernie was an excellent teacher. Beginning in the 1950s, Ernie gave microbiology lectures, taught laboratory skills and invariably provided a sympathetic ear to the students in his care. For 30 years, every medical student at Washington University had Ernie as a teacher and confidant: always available, always eager to help, but also firmly idealistic. Ernie provided students with a measure of encouragement, knowledge and idealism according to his high standards.

Despite his lack of formal training, Ernie was named a research assistant professor of microbiology in 1968, and four years later he was promoted to associate professor of microbiology with tenure. Over 100 colleagues sent let-

ters of support for his promotion, according to Joseph M. Davie, professor and head of department, microbiology and immunology and professor, department of pathology.

Simms is survived by his wife, Virginia and two children. Contributions may be made to the Ernie Simms Scholarship Fund, Washington University School of Medicine, Department of Microbiology and Immunology, Box 8093, 660 S. Euclid, St. Louis, MO 63110. The All Saints Episcopal Church, at 2831 N. Kingshighway, St. Louis, MO 63110 has also established a memorial fund.

In Memoriam (cont.)

1907

Grandison D. Royston, M.D., June 23, 1983

1912

Paul J. Ewerhardt, M.D., March 9, 1981

1917

Robert Mueller, M.D., January 5, 1983

1920

Sam B. Grant, M.D., November 14, 1982
Herman W. Meyer, M.D., March 28, 1983

1921

William B. Lewis, M.D., March 14, 1982
Herbert S. Pyne, M.D., February 27, 1982

1922

Theodore H. Hanser, M.D., November 11, 1983

1923

William L. Bradford, M.D., November 11, 1983

1924

Benedict A. Moranville, M.D., August 23, 1983
 Henry J. Ulrich, M.D., December 1, 1983

1925

Guy M. Maness, M.D., September 15, 1982
 Roy W. Robinson, M.D., June 15, 1983

1926

John M. McCaughan, M.D., July 21, 1982
 Caleb S. Stone, Jr., M.D., January 1, 1982

1927

Arthur C. Fortney, M.D., July 15, 1982
 Frank Glenn, M.D., January 12, 1982
 Victor L. Gould, M.D., July 11, 1983
 Arnold G. Klein, M.D., April 22, 1983

1928

Walter W. Baker, M.D., July 16, 1983
 John S. Harter, M.D., April 8, 1982
 Laurence L. Howard, M.D., May 30, 1983
 Oswald B. Schneidewind, M.D., October 13, 1982
 Arthur L. Stockwell, M.D., July, 1982
 Claude H. Zwart, M.D., August 18, 1983

1929

Frank A.C. Emery, M.D., April 21, 1983
 Gabriel A. Rivera, M.D., June 1, 1983

1932

Joseph R. Rebillot, M.D., August 13, 1983
 Albert M. Tocker, M.D., August 24, 1983

1933

Harry Goldman, M.D., April 25, 1982

Robert T. Terry, M.D., December, 1983
 Oreon K. Timm, M.D., June 2, 1982

1934

William W. Gist, M.D., June 18, 1983
 Mary M. Schmeckebier, M.D., September 7, 1982

1935

Heinz E. Haffner, M.D., October 22, 1982
 Augustin Jones, M.D., October 24, 1980
 Thomas McArtor, M.D., April 17, 1982
 Ben Senturia, M.D., July 7, 1982

1936

Ralph K. Earp, M.D., November 20, 1982
 Stephen S. Ellis, M.D., November 27, 1982
 William H. Jacobson, M.D., March 19, 1982
 Thomas E. McMillan, M.D., April 1, 1982
 Robert T. Tidrick, M.D., June 4, 1983

1937

Paul A. Brenner, M.D., September 8, 1983
 Carl E. Lischer, M.D., May 17, 1982
 Edgar H. Little, M.D., September 19, 1982
 William J. Quinn, M.D., October 26, 1982
 Thomas Russell, M.D., January 30, 1983

1938

Robert B. Lynn, M.D., September 4, 1983
 Winfield S. Wilder, M.D., November 27, 1982

1939

Mark J. Brockbank, M.D., August 17, 1982
 Sam Jones, M.D., July 13, 1982

1940

Albert Fleming, M.D., October 8, 1982
 Charles G. Obermeyer, M.D., August 24, 1983
 James H. Robertson, M.D., July 14, 1982

1941

John H. Beatty, M.D., August 15, 1983
 John G. Graybill, M.D., June 16, 1983
 John A. Putnam, M.D., December, 1982

1943

C.R. Mundy, M.D., February 23, 1983
 Ralph J. Smith, M.D., September 6, 1983

1944

Ivan E. Brown, M.D., November 3, 1982
 William H. Jolly, M.D., February 22, 1983

1945

Edmund V. Cowdry, Jr., M.D., August 30, 1982
 Donald L. Sweazy, M.D., September 2, 1983

1946

R. Robert Bates, M.D., June 4, 1983
 Victor B. Kieffer, M.D., May 13, 1983
 John W. Koehler, M.D., April 20, 1983

1947

Lee A. McNeel, Jr., M.D., May 26, 1982
 Arnold Namrow, M.D., March 12, 1982

1949

Gordon A. Munro, M.D., October 8, 1981
 John M. Ohtani, M.D., June 21, 1982
 Anthony J. Raso, M.D., April 4, 1982

1953

David R. Chiles, M.D., November 13, 1983
 Sun H. Lau, M.D., October 23, 1982

1954

Edward S. Reynolds, Jr., M.D., November 12, 1983

1955

Willard C. Schwartz, Jr., M.D., September 14, 1983

1976

Oliver Manigo, M.D., May 18, 1982
 Alan Tranishi, M.D., March 9, 1982

1982

Lorraine A. Johnsrud, M.D., May 6, 1983

Former House Staff

Seth S. Barnes, M.D., FHS, June 4, 1982
 Boyd K. Black, M.D., FHS, August 1, 1982
 Kenneth Fowler, M.D., FHS, July, 1982
 Robert S. Frech, M.D., FHS, December 19, 1982
 C.E. Gilliland, M.D., FHS, November 9, 1982
 Miriam Lending, M.D., FHS, September 13, 1983
 Gerald Levine, M.D., FHS, August 31, 1981
 Kevin C. Morrin, M.D., FHS, September 26, 1983
 William J. Natoli, M.D., FHS, August 11, 1981
 Charles H. Rammelkamp, M.D., FHS, December 1981
 Allen H. Sherman, M.D., FHS, March 16, 1982
 Stephen G. Sinclair, M.D., FHS, March 16, 1982
 Jung wan Kang, M.D., FHS, May 1, 1982
 Carl H. White, M.D., FHS, June 8, 1982

Researchers Decipher and Duplicate Atriopeptins

In an article published in the January 6 issue of *Science*, a team of researchers from Washington University in St. Louis and Monsanto report that they have deciphered and duplicated the molecular structures of chemicals produced in the heart which have profound effects on the kidney. The experiments detailed in the article may be the first steps in unmasking a new endocrine system, according to the researchers.

"What we are dealing with here is a chemical mechanism by which the heart and kidneys communicate, using a group of small peptides produced in the cardiac atria," says Philip Needleman, Ph.D., head of pharmacology at Washington University School of Medicine. "It seems that these peptides are released from the heart into the bloodstream, reach the kidney, and profoundly change the amount of sodium excreted and the amount of urine formed. In addition, they are powerful blood vessel relaxants. It seems a simple chemical or mixture of chemicals dramatically influences the [body's] whole internal fluid environment."

Needleman and his co-workers have dubbed the chemicals "Atriopeptins." "Atrio" refers to the atria, or upper chambers of the heart. "Peptins" are small fragments of protein.

Barbara Cole, M.D., a nephrologist and co-author of the *Science* article, says further study of the newly discovered communication

system will determine if its faulty operation might be responsible for some types of kidney, liver and heart malfunction as well as high blood pressure. "The heart's inability to produce and expel these peptides, or the kidney's inability to respond to them, might be the cause of some types of illness and may also provide new treatment for some illnesses which are currently resistant to therapy," says Cole. "I see many projects springing up based on this study."

According to Needleman, the investigation began when an inquisitive post-doctoral fellow working in the pharmacology department, Mark Currie, Ph.D., recognized a possible relationship between his own work with kidney cells and the work of a Canadian scientist, Adolfo J. De-Bold, who was experimenting with extracts taken from the cells of the upper chambers of the heart. In an experiment reported in *Science* in July 1983, Cole, Currie and David Geller, Ph.D., also from the pharmacology department, confirmed that injecting atrial extracts that had been purified into their individual elements caused laboratory animals to produce more urine, excrete more salt, and dilated blood vessels by relaxing their smooth muscle linings.

"What was discovered," Needleman concludes, "was a novel biology based on the heart's ability to sense an increase in salt concentration or blood volume and to — by way of these peptides — communicate those condi-



Researchers (from left) David Geller, Ph.D., Philip Needleman, Ph.D., Mark Currie, Ph.D., and Barbara Cole, M.D., examine a tracing that documents the biological activity of recently synthesized atriopeptins. These small peptides, synthesized naturally by the heart, affect the retention of Na^+ in the kidney and smooth muscle tone in blood vessels.

tions to the kidney where corrective measures could be taken. The whole system works in a circle, using positive and negative feedback between the kidneys and the heart."

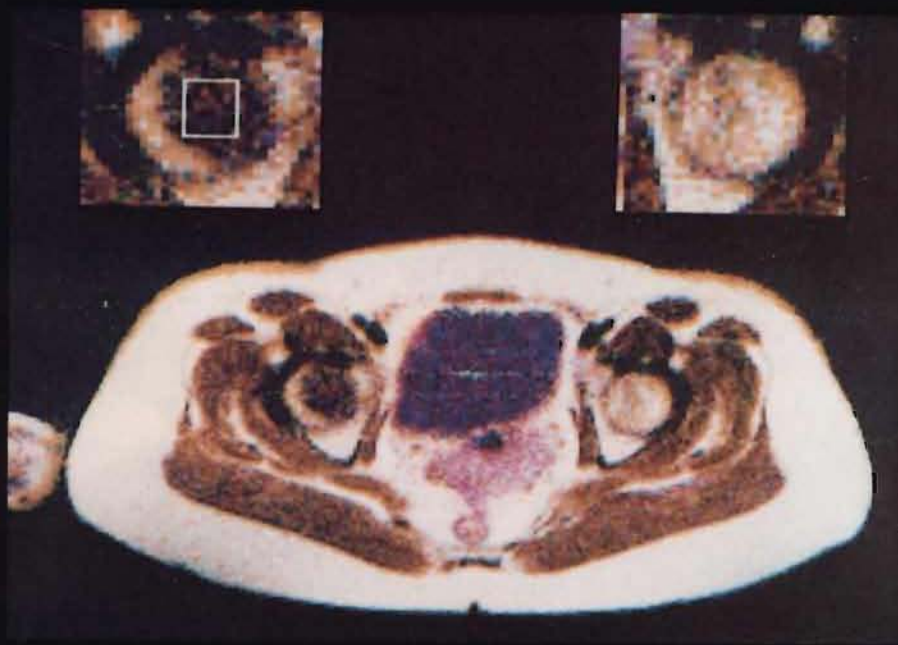
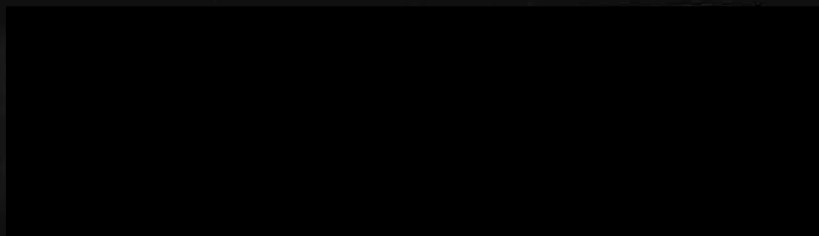
Examination of the atrial extracts showed that the effective chemicals were split into two groups of peptides, with one group containing slightly smaller peptide molecules than the other. Their January 6 *Science* report details the researchers' success at determining the exact makeup of the peptides that compose each group, the larger molecule having been dubbed Atriopeptin II, the smaller dubbed Atriopeptin I. With the assistance of the Protein Chemistry Group at Monsanto, the research team

was able not only to decipher the structure of Atriopeptins, but also to synthesize duplicate peptides that have the same biological activity as the original molecules.*

"So the essence of our collaboration here in St. Louis between Washington University and Monsanto is that we were able to go from crude atrial homogenates to animal testing of synthetic peptides in about six months' time," says Needleman.

Monsanto funded this research through the auspices of its \$23.5 million research contract with Washington University School of Medicine.

Washington University
School of Medicine
660 South Euclid Avenue
St. Louis, Missouri 63110



NASA technology was used to create this image, in which the hip pictured left is badly deteriorated. See story on page seven.



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